Translation

PCT/JP2003/015038

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PH-1953-PCT	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/JP2003/015038	International filing date (*day/month/year*) 25 November 2003 (25.11.2003)	Priority date (*day/month/year*) 26 May 2003 (26.05.2003)
International Patent Classification (IPC) or national classification and IPC C12N 15/11, 5/00, C12Q 1/06, C12N 7/00		
Applicant TORAY INDUSTRIES, INC.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☒ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) disc 1, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
01 July 2004 (01.07.2004)	20 January 2005 (20.01.2005)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2003/015038

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-21	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-21	NO
Industrial applicability (IA)	Claims	1-21	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

(Documents)

Document 1: Wakita, T. et al., "Idenshigata 2a no C-gata Kan'en Virus RNA Replicon on Juritsu," Dai 25 Kai The Molecular Biology Society of Japan Nenkai Program Koen Yoshishu, November 25, 2002, p. 386, Abst. No. W3aF-2

Document 2: EP 1043399 A2 (BARTENSCHLAGER, R.), 2003.10.11

Document 3: Ikeda, M. et al., "Selectable subgenomic and genome-length dicistronic RNAs derived from an infectious molecular clone of the HCV-N strain of hepatitis C virus replicate efficiently cultured Huh7 cells"
J. Virol., (2002 Mar), Vol. 76, No. 6, pp. 2997-3006

Document 4: Friebe, P. et al., "Sequences in the 5' nontranslated region of hepatitis C virus required for RNA replication"
J. Virol., (2001), Vol. 75, No. 24, pp. 12047-12057

Document 5: Lohmann, V. et al., "Replication of subgenomic hepatits C virus RNAs in a hepatoma cell line"
Science, (1999), Vol. 285, pp. 110-113

Document 6: WO 00/75338 A2 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA AS REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES), December 14, 2000

Document 7: JP 2002-171978 A (Zaidan Hojin Tokyo-To Igaku Kenkyu Kiko) June 18, 2002

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purpose of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

** If item 4 in Box No. I applies, the listing and /or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".*

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of Box V:

(Commentary)

1. Novelty and Inventive Step

a) Claims 1-16 and 21

In accordance with the article by Bartenschlager et al., document 1 describes the production of a replicon of the hepatitis C genotype 2a viral RNA, but it does not describe a concrete structure. Therefore, this examination finds that the inventions of the above claims are novel.

The article by Bartenschlager et al. described in document 1 corresponds to document 5. Document 5 describes the production of a replicon of the hepatitis C genotype 1b viral RNA, and that replicon contains a 5' untranslated region, the base sequences that encode the proteins NS3, NS4A, NS4B, NS5A and NS5B, a 3' untranslated region, the IRES sequence and a marker or reporter gene. In addition, the base sequence of the genome of HCV genotype 2a is already public knowledge from documents 6 and 7 (SEQ ID NO: 1). The base sequence identified in document 6 as SEQ ID NO: 1 contains mutations from A to G at site 6590 (corresponding to site 4936 of SEQ ID NO: 1 of this application) and from G to A at site 7505 (corresponding to site 5851 of SEQ ID NO: 1 of this application).

Therefore, this examination finds that persons skilled in the art could easily prepare an RNA replicon similar to that described in document 5 for HCV genotype 2a. Moreover, this examination finds that persons skilled in the art could easily conceive of a screening method, etc. utilizing the same.

As a result, the inventions of claims 1-16 and 21 lack an inventive step.

b) Claims 1-21

Documents 2-5 describe a replicon of the hepatitis C genotype 1b viral RNA that a 5' untranslated region, the base sequences that encode the proteins NS3, NS4A, NS4B, NS5A and NS5B, a 3' untranslated region, the IRES sequence and a marker or reporter gene, a process for producing the same, and a method for obtaining a replicon mutant with an increased replication efficiency by subculturing the above replicon through at least one passage (see claims 12 and 13 of document 2).

On the other hand, this examination finds that the problem of obtaining RNA replicons for genotypes other than genotype 1b was well known to persons in the art (if necessary, see document 5, page 1972, center column, Par. No. 2, for example), and because the genomic DNA of genotype 2a had already been analyzed (documents 6 and 7), persons skilled in the art could easily conceive of producing a RNA replicon having a similar structure for genotype 2a. As noted above, the base sequence identified as SEQ ID NO: 1 in document 6 has several point mutations, and persons skilled in the art can select as needed an RNA replicon having such mutations that is suitable for insertion into cultured cells. In a similar manner, persons skilled in the art can easily prepare a screening method utilizing the same.

As a result, the inventions of claims 1-21 lack an inventive step.

2. Industrial Applicability

The inventions of claims 1-21 have industrial applicability.